REMARKS

This is responsive to the final Office Action mailed May 27, 2005.

Applicant has canceled claims 11 and 12. Claim 1 has been amended to provide a preparation that includes an adhesive layer prepared by heat-melting or dissolving in a solvent a drug composition and then spreading the adhesive layer. Support for this amendment is found in the specification at page 13, line 19 – page 14, line 1, and in the Examples, e.g., on pages 15-22. New claims 13-18 have been added. Basis for the addition of these claims is found, for example, in original claims 2-6. No new matter has been added.

Applicant thanks the Examiner for the courtesy of an interview.

Rejections Under 35 U.S.C. 103

The Examiner rejected claims 1-12 under 35 U.S.C. § 103 as unpatentable over three separate references: JP 08-157365, JP 10-045570 and US patent 5,866,157. Each of the rejections has the same basis, namely that the reference teaches a percutaneous adhesive preparation in which the disclosed thickness of an adhesive film implies that particle size of powdered organic acid cannot be more than 100 micrometers in diameter. The Examiner suggests that one of ordinary skill in the art would have been motivated to select sodium acetate having particle sizes less than 50 micrometers (or 100 micrometers on page 6 of the Office Action) motivated by the references' teaching that "such preparation has remarkable high skin permeation rate and remarkable reduced skin irritation." (Office Action at p.4, similar recitations on pages 5 and 6). Applicant respectfully requests reconsideration.

The references do not teach the invention

The Examiner acknowledges that the references do not expressly disclose that the organic acid is in powder form, and if so, a particular diameter or range of diameters of particles. Thus there is no explicit "teaching" of preparations having particle sizes of less than 100 μm or less than 50 μm as suggested by the Examiner. The Examiner indicated that this teaching was

implied from the thickness of the adhesive film that contains the components of the preparations recited in the references.

Applicant respectfully disagrees that the teaching of the references implies any particle size, let alone the particle size recited in the instant claims. The products disclosed in the cited references are most likely prepared by a process comprising heat melting or dissolving raw materials in solvent. Therefore, the adhesive film of the cited references, which is 50-100 μm thick, can easily be made from raw materials of any particle size, including organic acid salts particles having more than 100 μm in diameter. Accordingly, the fact that the cited references disclose an adhesive film having a thickness of 50-100 μm is not a teaching or suggestion that the particle size of the organic acid salt is less than 100 μm in diameter.

Although these references have no explicit description of particle size used, the average particle size of commercially abailable sodium acetate is in general not less than about 500 μm as described in the specification at page 7, lines 10-12.

Further, as shown by the Elias and Johnson references (enclosed herewith), the width of the intercellular space between corneocytes is much smaller than 0.1 μm, which means that one of ordinary skill in the art would not have predicted that the claimed particle size (0.1-100 μm) can affect skin permeability of a base drug salt. In particular, Elias states that "The width of the intercellular space spanning adjacent cells under these conditions varies from 60 to 100 nm." Page 185, left column, lines 15-18. Johnson shows in Figure 1 that the gaps between keratinocytes is about 75 nm. See also page 1164, right column, line 10.

Given these distances, it is entirely unexpected that the claimed invention, which is characterized not by the particle size of the base drug salts *per se* but by that of the organic acid salts. The particle size of the organic acid salts as claimed, 0.1-100 μm, is not small enough to be absorbed into the skin, but forms an ion pair with base drug salts that unexpectedly enhances transdermal absorption. These superior unexpected properties are described in the application on page 4, lines 9-19, and the experimental data presented in Figs. 1-3 clearly show such an advantageous effect.

There is no motivation to modify the teachings of the references

The Examiner suggests that one of ordinary skill in the art would be motivated to use particles of less than 50 μm or 100 μm by the teaching of the references of high skin permeation rates and reduced skin irritation. Applicant respectfully disagrees.

Taking the '157 patent as an example, there is no teaching whatsoever of particle sizes; the Examiner has implied that the reference teaches particles of a particular size. Even if this were sufficient to teach one of ordinary skill in the art, which Applicant has disputed above, it is not a sufficient teaching to motivate the skilled artisan to use particles of that diameter, because there is no link between particle size and effect made in the '157 patent. The '157 patent attributes the enhanced effects of the invention to "formulating a physiological active substance, an organic acid and an absorption enhancer into an adhesive layer of a matrix type patch formulation." See col. 2, lines 33-38.

In contrast, the present Applicant has clearly identified the effects of the organic acid salt powder of the claimed size. No person of ordinary skill would have expected, from the prior art cited, that particles of the claimed size would result in the ion-pair formation which brings superior properties such as improving solubility of the drug to the skin (page 4, lines 9-19) and percutaneous drug-absorbance effect (page 4, line 24 to page 5, line 1). These advantageous effects are clearly demonstrated by the working examples and comparative examples in the present specification.

Therefore one of ordinary skill in the art would not be motivated to use organic acid salt size powder having particle sizes in the claimed range. Thus, the non-obviousness of the present invention vis-à-vis the cited prior art should be affirmed.

In view of the foregoing, withdrawal of the rejections of the claims as unpatentable over JP 08-157365, JP 10-045570 or US patent 5,866,157 under 35 U.S.C. 103 is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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